

CLAIMS

1. A process for preparing a salt of (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol that comprises:
mixing i) a sample comprising (-)-(2R, 3R)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol ((2R, 3R) enantiomer), ii) at least one solvent having a boiling point of at least 50°C and iii) 1.1 equivalent or higher of L-DTTA in any order, heating the mixture to at least 50°C for at least 1 hour to form crystals comprising an L-DTTA salt of (+)-(2S, 3S)-2-(3-chlorophenyl)-3,5,5-trimethyl-2-morpholinol ((2S, 3S) enantiomer), and isolating the crystals, wherein the yield of the L-DTTA salt of the (2S, 3S) enantiomer is greater than 50% based on said sample.
2. The process according to claim 1, wherein the solvent preferably dissolves the L-DTTA salt of the (2R, 3R) enantiomer over the L-DTTA salt of the (2S, 3S) enantiomer.
3. The process according to claim 1 or claim 2, wherein the solvent is at least one selected from alkyl acetate, dialkyl ketone, and nitrile.
4. The process according to claim 3 wherein the solvent is ethyl acetate.
5. The process according to claim any one of claims 1 to 4, wherein the amount of L-DTTA is 1.2-2.0 equivalents.
6. The process according to any one of claims 1 to 5, wherein the mixture of the sample comprising the (2R, 3R) enantiomer, solvent and L-DTTA is heated to reflux.
7. The process according to any one of claims 1 to 6, wherein the mixture is heated for at least 5 hours.
8. The process according to any one of claims 1 to 7, wherein the crystals are essentially enantiomerically pure with respect to the (2S, 3S) enantiomer.
9. The process according to any one of claims 1 to 8, which is a continuous process.
10. The process according to any one of claims 1 to 9, wherein the sample comprising the (2R, 3R) enantiomer is a racemic mixture of the (2R, 3R) enantiomer and the (2S, 3S) enantiomer.
11. The process according to any one of claims 1 to 9, wherein the sample comprising the (2R, 3R) enantiomer is a non-racemic mixture of the (2R, 3R) enantiomer and the (2S, 3S) enantiomer.

12. The process according to any one of claims 1 to 9, wherein said sample comprising the (2R, 3R) enantiomer contains at least 50wt% of the (2R, 3R) enantiomer based on the weight of said sample.
13. The process according to any one of claims 1 to 9, wherein the sample comprising the (2R, 3R) enantiomer is essentially enantiomerically pure (2R, 3R) enantiomer.
14. The process according to any one of claims 1 to 13, wherein said sample comprising the (2R, 3R) enantiomer is formed in a step comprising reacting 2-bromo-3'-chloropropiophenone with 2-amino-2-methylpropanol.
15. The process according to any one of claims 1 to 14, further comprising a step of converting the L-DTTA salt of the (2S, 3S) enantiomer to another salt which is pharmaceutically acceptable.
16. The process according to claim 15, wherein the other salt is a hydrochloride salt.